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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/287,632	04/07/1999	PETER MICHAEL WATERHOUSE	021565-060	6526
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EXAMINER ZARA, JANE J				
ART UNIT 1635		PAPER NUMBER		
NOTIFICATION DATE 09/19/2008		DELIVERY MODE ELECTRONIC		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com

# Office Action Summary

## Application No.

09/287,632

## Applicant(s)

WATERHOUSE ET AL.

## Examiner

Jane Zara

## Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 07 May 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-10, 12, 22, 26, 40, 42-44, 46, 50, 53, 54, 56, 58 and 63-134 is/are pending in the application.
- 4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 22, 26, 42, 53, 54, 56, 58, 63-69, 85-97, 100-103, 106-110, 115-122, 127-134 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-84C)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

Continuation of Disposition of Claims: Claims withdrawn from consideration are 1-10,12,40,43,44,46,50,70-84,98,99,104,105,111-114 and 123-126.

### **DETAILED ACTION**

This Office action is in response to the communications filed 5-7-08.

Claims 1-10, 12, 22, 26, 40, 42-44, 46, 50, 53, 54, 56, 58, 63-134 are pending in the instant application. Claims 1-10, 12, 40, 43, 44, 46, 50, 70-84, 98, 99, 104, 105, 111-114, 123-126 are withdrawn as being drawn to a non-elected invention, and claims 22, 26, 42, 53, 54, 56, 58, 63-69, 85-97, 100-103, 106-110, 115-122, 127-134 have been examined on their merits as set forth below.

The declaration under 37 CFR 1.132 filed 5-7-08 are insufficient to overcome the rejection of claims 22, 26, 42, 53, 54, 56, 58, 63-69, 85-97, 100-103 and 106-110, 115-122, 127-134 based upon 35 U.S.C. 112, first paragraph as set forth in the last Office action and for the reasons set forth below.

Applicant's arguments with respect to the 35 U.S.C. 102 and 103(a) rejections have been considered but are moot in view of the new ground(s) of rejection set forth below.

### ***Response to Arguments and Amendments***

#### **Withdrawn Rejections**

Any rejections not repeated in this Office action are hereby withdrawn.

#### **Maintained Rejections**

Claims 22, 26, 42, 53, 54, 56, 58, 63-69, 85-97, 100-103 and 106-110, 115-122, 127-134 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the

written description requirement for the reasons of record set forth in the Office action mailed 11-1-07 and for the reasons set forth below.

Applicant's arguments and declarations filed 5-7-08 have been fully considered but they are not persuasive. The claims are drawn to plants, eukaryotic cells, and chimeric DNA comprising an operable promoter, transcription termination and polyadenylation region, and further comprising a DNA region encoding a region capable of forming an artificial hairpin RNA structure with a double stranded RNA stem by base pairing between regions with a sense and an antisense nucleotide sequence, which sense nucleotide sequence includes at least 20, 50, 100, or 550 consecutive nucleotides having 100% sequence identity with at least 20, 50, 100, or 550 consecutive nucleotides of a nucleic acid of interest, and which antisense sequence includes at least 20, 50, 100, or 550 consecutive nucleotides having 100% sequence identity with said at least 20, 50, 100, or 550 consecutive nucleotides of the sense sequence, and which chimeric DNA further comprises any intron.

Applicant argues that adequate written description has been provided for the claimed invention at the time of filing, and that a person of ordinary skill in the art would have recognized that the inventors were in possession of the broad genus of compounds and plants claimed. Applicant provides various publications defining introns and that the claims now broadly encompass introns, implicating those involved in the

excision or splicing process, rather than the broad genus comprising intronic sequences.

The initial disclosure teaches fully complementary pair constructs for reducing the phenotypic expression of a transgenic Gus gene (of approximately 1580 base pairs), and complementary pair constructs for reducing the phenotypic expression of the  $\Delta 12$  desaturase target gene in *Arabidopsis* (of approximately 620 base pairs) which complementary pair constructs additionally comprise the pyruvate orthophosphate dikinase 2 intron 2 from *Flaveria trinervia* (SEQ ID NO. 7) in forward or reverse orientation.

These examples that have been provided in the initial disclosure, however, are representative of the very broad genus of compounds and plants claimed, which encompass any plants, eukaryotic cells, or chimeric DNA comprising an operable promoter, transcription termination and polyadenylation region, and further comprising any DNA region encoding a region capable of forming an artificial hairpin RNA structure with a double stranded RNA stem by base pairing between regions with a sense and an antisense nucleotide sequence, which sense nucleotide sequence includes at least 20, 50, 100, or 550 consecutive nucleotides having 100% sequence identity with at least 20, 50, 100, or 550 consecutive nucleotides of a nucleic acid of interest, and which antisense sequence includes at least 20, 50, 100, or 550 consecutive nucleotides having 100% sequence identity with said at

least 20, 50, 100, or 550 consecutive nucleotides of the sense sequence, and which chimeric DNA further comprises any intron. Applicant, by providing the examples described above, were not in possession of this broad array of compounds or plants at the time of filing. The instant rejection is hereby maintained.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 22, 26, 42, 53, 54, 56, 58, 63-69, 85-97, 100-103, 106-110, 115-122, 127-134 are rejected under 35 U.S.C. 103(a) as being unpatentable over Flavell, Metzclaff et al, and Stam et al, the combination in view of Brown et al, Lusky et al.

The claims are drawn to plants, eukaryotic cells, and chimeric DNA comprising an operable promoter, transcription termination and polyadenylation region, and further comprising a DNA region encoding a region capable of forming an artificial hairpin RNA structure with a double stranded RNA stem by base pairing between regions with a sense and an antisense nucleotide sequence, which sense nucleotide sequence includes at least 20 consecutive nucleotides having 100% sequence identity with at least 20 consecutive nucleotides of a nucleic acid of interest, and which antisense sequence includes at least 20 consecutive nucleotides having 100% sequence identity with said at least 20 consecutive nucleotides of the sense sequence, and which chimeric DNA further comprises any intronic sequence.

Flavell (Proc. Natl. Acad. Sci., Vol. 91, pages 3490-3496, 1994) teaches plants, eukaryotic cells, and chimeric DNA comprising an operable promoter, transcription termination and polyadenylation region, and further comprising a DNA region encoding a region capable of forming a double stranded RNA stem by base pairing between regions with a sense and an antisense nucleotide sequence, which sense nucleotide sequence includes at least 10 consecutive nucleotides having 100% sequence identity with at least 10 consecutive nucleotides of a nucleic acid of interest, and which antisense sequence includes at least 10 consecutive nucleotides having 100% sequence identity with said at least 10 consecutive nucleotides of the sense sequence (see esp. the abstract and text on pp. 3490-3491).



Metzlaff et al (Cell, Vol. 88, pages 845-854, 1997) teach plants, eukaryotic cells, and chimeric DNA comprising an operable promoter, transcription termination and polyadenylation region, and further comprising a DNA region encoding a region capable of forming a double stranded RNA by base pairing between regions with a sense and an antisense nucleotide sequence (see esp. fig. 1 and 2 on p. 846; Table 1 and text on p. 849; text on p. 850; fig. 7 on p. 852).

Stam et al (Annals of Botany, Vol. 79, pages 3-12, 1997) teach plants, eukaryotic cells, and chimeric DNA comprising an operable promoter, transcription termination and polyadenylation region, and further comprising a DNA region encoding a region capable of forming an artificial hairpin RNA structure with a double stranded RNA stem by base pairing between regions with a sense and an antisense nucleotide sequence, which sense nucleotide sequence includes at least 10 consecutive nucleotides having 100% sequence identity with at least 10 consecutive nucleotides of a nucleic acid of interest, and which antisense sequence includes at least 10 consecutive nucleotides having 100% sequence identity with said at least 10 consecutive nucleotides of the sense sequence, (see esp. bridging paragraph on pp. 3-4; fig. 1 on p. 4; text on page 8; fig. 3 on p. 9).

The primary references of Flavell, Metzlaff et al and Stam et al do not teach double stranded hairpin constructs in their inverted repeats, nor do they teach the insertion of an intron in their double stranded inhibitory constructs.

Brown et al (USPN 5,859,347) teach plant cells transformed with chimeric nucleic acid expression constructs expressing desired DNA sequences, and which expression constructs comprise expression elements including operably linked promoters and further comprising heterologous introns, which introns enhance stability and expression of the nucleic acid sequences in an expression construct (see col. 8, line 53-col. 9, line 17, examples 1-7 in cols. 10-18 and figures 8-27).

Lusky et al (USPN 6,350,575) teach expression constructs comprising antisense RNA and further comprising an intron as well as other expression elements including translation termination and polyadenylation signals (col. 6, line 15-col. 7, line 14).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to alter the expression of a target gene of known sequence, which gene is either endogenous or heterologous to a plant cell, which target gene is either stably integrated or extrachromosomal, comprising the introduction of nucleic acids comprising sense and complementary antisense sequences of the target gene, which are operably linked to a constitutive or heterologous promoter, and which are optionally expressed on separate or the same expression construct, and hybridize after their expression in the cell to the complementary sequences of each other to form a double stranded molecule, whereby a duplex is formed between the expressed sense and antisense fragments, because this approach to gene silencing had been proposed and studied previously by Flavell, Metzlauff et al and Stam et al. One of ordinary skill in the art would have reasonably expected the expressed double stranded RNA to target and inhibit the expression of corresponding target sequences of a target gene of known

sequence, because the correlation between gene silencing and the presence of these self complementary nucleic acid sequences were taught previously by Flavell, Metzlaff et al and Stam et al. One of ordinary skill in the art would have been motivated to design inverted repeats as a single molecule to test its inhibitory capacity because expression of a single, contiguous self annealing construct would provide for more efficient self annealing compared to two separately expressed self annealing molecules, applying scientific logic to the teachings of Flavell, Metzlaff and Stam concerning the ability of inverted repeats and self annealing, complementary nucleic acids to provide for target gene suppression.

One of ordinary skill in the art would have been motivated to include intronic sequences within the expression constructs for gene expression in plants because the use of intronic sequences for enhancing vector stability and hence enhance expression of a desired gene in cells had been taught previously by Brown et al. Furthermore, Lusky et al also teaches the incorporation of intronic sequences in expression constructs and it was well known in the art that the inclusion of introns enhances the expression of RNA in plants. One of ordinary skill in the art would have optionally placed the intronic sequences between the sense and antisense sequences in the inhibitory, double stranded, self complementary constructs originally taught Flavell, Metzlaff and Stam because this is a design choice. One of ordinary skill in the art would have expected that the intronic sequences, inserted at different places in the expression construct, would enhance expression of the chimeric constructs in plants and it would take routine experimentation to determine where in the construct the intron sequences

would be inserted, as long as complementarity between the sense and antisense sequences was maintained for target gene suppression, as taught previously. It would have taken routine experimentation and design choice to alter the length of the self complementary molecules which targeted the target of interest.

One of ordinary skill in the art would have been motivated to inhibit the expression of target genes by these expressed RNAi molecules, for altering cellular phenotypes in order to study gene function, or to study the role of various target genes by comparing cellular processes in the absence or presence of these target genes' expression, or to inhibit a deleterious pathogenic gene of an invading organism in a plant cell by inhibiting pathogenic target gene expression using this technique of gene silencing. One of ordinary skill in the art would have expected that the inclusion of intronic sequences would enhance expression construct stability because the inclusion of intronic sequences in expression constructs was routine in the art, as evidenced by the inclusion of intronic sequences in commercial and other published expression constructs, at the time the invention was made. One of ordinary skill in the art would have expected that the transformation of expression cassettes for target gene silencing in appropriate plant cells, whereby the concerted expression of both the sense and antisense fragments in appropriate target cells using appropriate promoters is obtained, leads to the formation of double stranded fragments directed to the target gene sequences in the transformed cells, and consequently interferes with the expression of the target gene, thereby producing inhibition of target gene expression, allowing a

comparison of cellular phenotypes in the presence and absence of target gene inhibition, as taught previously by Flavell, Metzloff and Stam.

Therefore the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

### ***Conclusion***

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. ' 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jane Zara whose telephone number is (571) 272-0765. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz, can be reached on (571) 272-0763. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

**Jane Zara**  
**9-12-08**

**/Jane Zara/**

**Primary Examiner, Art Unit 1635**